

We claim:

1. A milnacipran formulation that provides pulsatile release of milnacipran to produce a therapeutic effect over approximately 24 hours when administered to a patient in need, with diminished incidence and reduced intensity relative to one or more immediate release milnacipran side effects.
2. The milnacipran formulation according to Claim 1, wherein the side effect is nausea.
3. The malnacipran formulation according to Claim 1, wherein the side effects are selected from the group consisting of vomiting, headache, tremulousness, anxiety, panic attacks, palpitations, urinary retention, orthostatic hypotension, diaphoresis, chest pain, rash, weight gain, back pain, constipation, vertigo, increased sweating, agitation, hot flushes, tremors, fatigue, somnolence, dyspepsia, dysoria, nervousness, dry mouth, abdominal pain, irritability, and insomnia.
4. The milnacipran formulation according to Claim 1 comprising:
 - (a) an immediate release dosage unit comprising a first dose of the active agent that is released substantially immediately following oral administration of the dosage form to a patient resulting in the first plasma level peak at approximately 0.05 hours to less than 3 hours following oral administration;
 - (b) a delayed release dosage unit comprising a second dose of the active agent and a means for delaying release of the second dose resulting in the second plasma level peak at approximately 3 hours to less than 14 hours following oral administration of the dosage form; and optionally
 - (c) a second delayed release dosage unit comprising a third dose of the active agent and a means for delaying release of the third dose resulting in the third plasma level peak at approximately 5 hours to less than 18 hours following oral administration of the dosage form.
5. The milnacipran formulation according to Claim 4 wherein an enteric coating is added to the formulation and the release profile is further characterized by a 0.05-4 hours lag time period during which less than

approximately 10% of the first “pulse” milnacipran dose is released followed by a complete release of the first “pulse”.

6. The milnacipran formulation according to Claim 1 providing milnacipran blood plasma levels that are characterized by C_{\max} below approximately 3000 ng/ml.

7. The milnacipran formulation according to Claim 6 providing milnacipran blood plasma levels that are characterized by C_{\max} below approximately 2000 ng/ml.

8. The milnacipran formulation according to Claim 6 providing milnacipran blood plasma levels that are characterized by C_{\max} below approximately 1000 ng/ml.

9. The milnacipran formulation according to Claim 1 further comprising at least one other active compound selected from the group consisting of analgesics, anti-inflammatory drugs, antipyretics, antidepressants, antiepileptics, antihistamines, antimigraine drugs, antimuscarinics, anxiolytics, sedatives, hypnotics, antipsychotics, bronchodilators, anti asthma drugs, cardiovascular drugs, corticosteroids, dopaminergics, electrolytes, gastro-intestinal drugs, muscle relaxants, nutritional agents, vitamins, parasympathomimetics, stimulants, anorectics, and anti-narcoleptics.

10. The milnacipran formulation according to Claim 9 comprising one or more compounds selected from the group consisting of aceclofenac, acetaminophen, adomoxetine, almotriptan, alprazolam, amantadine, amcinonide, aminocyclopropane, amitriptyline, amolodipine, amoxapine, amphetamine, aripiprazole, aspirin, atomoxetine, azasetron, azatadine, beclomethasone, benactyzine, benoxaprofen, bermoprofen, betamethasone, bicifadine, bromocriptine, budesonide, buprenorphine, bupropion, buspirone, butorphanol, butriptyline, caffeine, carbamazepine, carbidopa, carisoprodol, celecoxib, chlordiazepoxide, chlorpromazine, choline salicylate, citalopram, clomipramine, clonazepam, clonidine, clonitazene, clorazepate, clotiazepam, cloxazolam, clozapine, codeine, corticosterone, cortisone, cyclobenzaprine, cyproheptadine, demexiptiline, desipramine, desomorphine, dexamethasone, dexanabinol,

dextroamphetamine sulfate, dextromoramide, dextropropoxyphene, dezocine, diazepam, dibenzepin, diclofenac sodium, diflunisal, dihydrocodeine, dihydroergotamine, dihydromorphine, dimetacrine, divalproxex, dizatriptan, dolasetron, donepezil, dothiepin, doxepin, duloxetine, ergotamine, escitalopram, estazolam, ethosuximide, etodolac, femoxetine, fenamates, fenoprofen, fentanyl, fludiazepam, fluoxetine, fluphenazine, flurazepam, flurbiprofen, flutazolam, fluvoxamine, frovatriptan, gabapentin, galantamine, gepirone, ginko bilboa, granisetron, haloperidol, huperzine A, hydrocodone, hydrocortisone, hydromorphone, hydroxyzine, ibuprofen, imipramine, indiplon, indomethacin, indoprofen, iprindole, ipsapirone, ketaserin, ketoprofen, ketorolac, lesopitron, levodopa, lipase, lofepramine, lorazepam, loxapine, maprotiline, mazindol, mefenamic acid, melatonin, melitracen, memantine, meperidine, meprobamate, mesalamine, metapramine, metaxalone, methadone, methadone, methamphetamine, methocarbamol, methyldopa, methylphenidate, methylsalicylate, methysergid(e), metoclopramide, mianserin, mifepristone, milnacipran, minaprine, mirtazapine, moclobemide, modafinil, molindone, morphine, morphine hydrochloride, nabumetone, nadolol, naproxen, naratriptan, nefazodone, neurontin, nomifensine, nortriptyline, olanzapine, olsalazine, ondansetron, opipramol, orphenadrine, oxaflozane, oxaprazin, oxazepam, oxitriptan, oxycodone, oxymorphone, pancrelipase, parecoxib, paroxetine, pemoline, pentazocine, pepsin, perphenazine, phenacetin, phendimetrazine, phenmetrazine, phenylbutazone, phenytoin, phosphatidylserine, pimozide, pirlindole, piroxicam, pizotifen, pizotyline, pramipexole, prednisolone, prednisone, pregabalin, propanolol, propizepine, propoxyphene, protriptyline, quazepam, quinupramine, reboxitine, reserpine, risperidone, ritanserin, rivastigmine, rizatriptan, rofecoxib, ropinirole, rotigotine, salsalate, sertraline, sibutramine, sildenafil, sulfasalazine, sulindac, sumatriptan, tacrine, temazepam, tetrabenazine, thiazides, thioridazine, thiothixene, tiapride, tiasipirone, tizanidine, tofenacin, tolmetin, toloxatone, topiramate, tramadol, trazodone, triazolam, trifluoperazine, trimethobenzamide, trimipramine, tropisetron, valdecoxib, valproic acid, venlafaxine, viloxazine, vitamin E, zimeldine,

ziprasidone, zolmitriptan, zolpidem, zopiclone and isomers, salts, and combinations thereof.

11. The milnacipran formulation according to Claim 1, wherein the milnacipran is in the form of a therapeutically equivalent dose of dextrogyral or levrogyral enantiomers of the milnacipran or pharmaceutically acceptable salts thereof.
12. The milnacipran formulation according to Claim 1, wherein the milnacipran is in the form of a therapeutically equivalent dose of a mixture of milnacipran enantiomers or pharmaceutically acceptable salts thereof.
13. The milnacipran formulation according to Claim 1, wherein the milnacipran is in the form of a therapeutically equivalent dose of the active metabolite of milnacipran or pharmaceutically acceptable salts thereof.
14. The milnacipran formulation according to Claim 1, wherein the milnacipran is in the form of a therapeutically equivalent dose of para-hydroxy-milnacipran (F2782) or pharmaceutically acceptable salts thereof.
15. The milnacipran formulation according to Claim 1 comprising an enteric coating.
16. The milnacipran formulation according to Claim 1, wherein the administrable milnacipran unit dose is from 25 to 500 mg.
17. The milnacipran formulation according to Claim 1, wherein the administrable milnacipran unit dose is from 200 to 500 mg.
18. The milnacipran formulation according to Claim 9 comprising 25 to 500 mg milnacipran and 100 to 600 mg modafinil.
19. The milnacipran formulation according to claim 1 comprising a mixture of beads or particles releasing drug at different times.
20. A kit comprising the milnacipran formulation of Claim 1.
21. The kit of Claim 20 comprising different dosage units of milnacipran to allow for dosage escalation.
22. The kit of Claim 20 comprising instruction on taking the formulation once daily before bedtime.

23. A method of making a milnacipran formulation comprising providing the formulation of Claim 1.

24. A method for delivering a therapeutic dose of milnacipran as a starting dose to a patient in need thereof, with diminished incidence or reduced intensity of common milnacipran side effects, comprising administering to the patient in need thereof the milnacipran formulation of claim 1.